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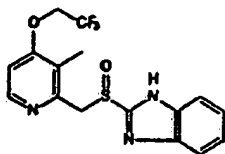
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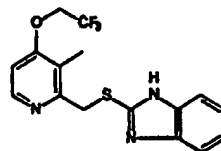
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(54) Title: PROCESS FOR PREPARING SULFOXIDE COMPOUNDS



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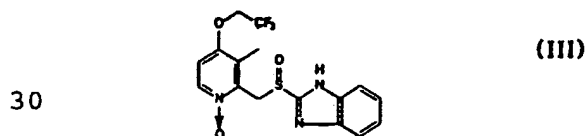
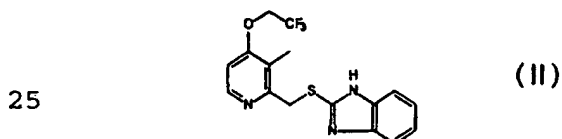
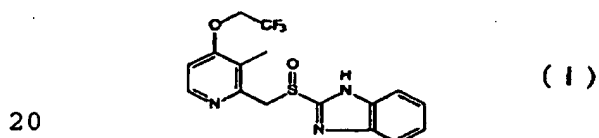
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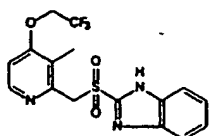
(57) Abstract: Disclosed herein is a process of preparing a sulfoxide compound of the formula (I) useful as an anti-ulcer agent at high yield and purity. This process comprises reacting a sulfide compound of the formula (II) with hydrogen peroxide in an ethanol solvent in the presence of a rhenium catalyst of 1 to 5 mol % relative to the sulfide compound (II).

PROCESS FOR PREPARING SULFOXIDE COMPOUNDS

TECHNICAL FIELD

The present invention relates to a process for preparing sulfoxide compounds useful as anti-ulcer agents having a gastric acid secretion inhibiting action. More particularly, the present invention relates to a process for preparing a sulfoxide compound of the formula I, which comprises the step of oxidizing a sulfide compound of the formula II with hydrogen peroxide in the presence of a rhenium compound acting as a catalyst. Unlike the prior art, the process of the present invention minimizes a production of an N-oxide by-product of the formula III and an sulfone by-product of the formula IV and thus produces the sulfoxide compound of the formula I at high yield and purity using a simple isolation procedure.



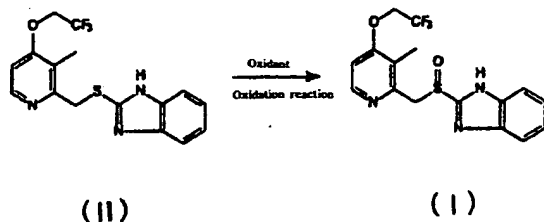


(IV)

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The sulfoxide compound represented by the formula I is useful as an anti-ulcer agent having a gastric acid secretion inhibiting action. Generally, the sulfoxide compound of the formula I is prepared by oxidizing the sulfide compound of the formula II with an oxidizing agent, as indicated in the following Scheme 1:

Scheme 1



15

(II)

(I)

BACKGROUND ART

20

Oxidizing agents previously disclosed in the art for the oxidation of the sulfide compound include iodosobenzene (Spanish Patent No. 539,793 (1985)), iodosomethylbenzene (Spanish Patent No. 540,147 (1985)), m-chloroperbenzoic acid (US Patent No. 4,628,098 (1986) and 4,255,431 (1981)), peracetic acid (WO 98/09962 (1998)), sodium hypochlorite (EP 268,956 (1988)), sodium periodate (Spanish Patent No. 550,070 (1985)) and the like. However, m-chloroperbenzoic acid is usually used in view of its activity and easiness of weighing.

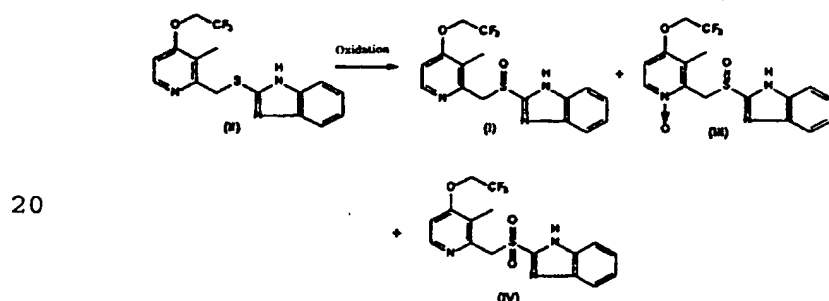
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The prior art for preparing the sulfoxide compound I by an oxidation of the sulfide compound II with m-chloroperbenzoic acid will now be described.

Korean Patent No. 052837 (1992) describes only a melting point of the compound I without descriptions of a purity and yield of the compound I. However, Example of Korean Patent No. 100796 (1996) describes preparing the compound I at a relatively low yield of 74.9%.

The reason why the compound I is produced at such a low yield is that an oxidation of the compound II with m-chloroperbenzoic acid as an oxidizing agent results in byproducts such as N-oxide of the formula III and a sulfone compound of the formula IV, as shown in the following Scheme 2:

15 Scheme 2



Another reason for the low yield is that the produced byproducts are very similar in physical and chemical properties, such as solubility, to those of the sulfoxide compound I and thus is not easily removed by a usual purification method such as recrystallization. Also, the oxidation with m-chloroperbenzoic acid is disadvantageous in that m-chloroperbenzoic acid is an expensive reagent and is a dangerous substance requiring

cautions during its use and storage so that it is difficult to be handled in large quantities. Further, the oxidation with m-chloroperbenzoic acid has a drawback when being applied for industrial purpose, because it utilizes environmentally harmful halogenated solvents such as chloroform, methylene chloride and the like.

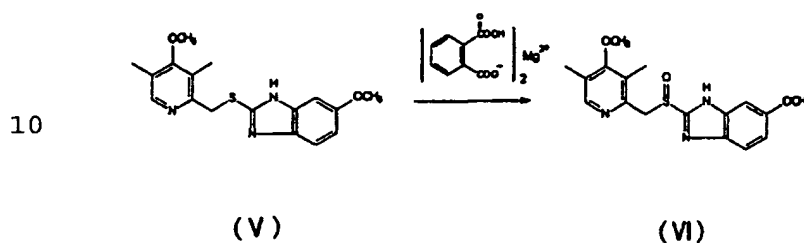
In addition, Japanese Patent Application Laid Open No. Heisei 11-71370 (1999) discloses a process of preparing the sulfoxide compound I by oxidizing the sulfide compound II in a mixed solvent of nonpolar solvent and lower alcohol. However, this process is reported as producing the sulfoxide compound I at a low yield of 71.6%. Moreover, WO 99/02521 (1999) describes oxidizing the sulfide compound II with sodium perborate tetrahydrate ($\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$) in the presence of anhydrous acetic acid and water to produce the sulfoxide compound I at a yield of 78.4%. An alternative process in the latter publication includes oxidizing the sulfide compound II with N-chlorosuccinic acid in the presence of an inorganic base to produce the sulfoxide compound I at a yield of 84.1%.

The above-described prior processes using an oxidizing agent such as m-chloroperbenzoic acid are difficult to be applied for the industrial purpose. This is because the oxidizing agent used is an expensive reagent and, in many cases, a reaction is not proceeded during the oxidation procedure, or decomposition products or by-products are produced in large quantities.

Recently, Korean Patent Publication No. 92-3691 (1992) and US Patent No. 5,391,752 (1995) have disclosed

processes for preparing omeprazole of the formula VI, which comprise the step of reacting a sulfide compound of the formula V with magnesium monoperoxyphthalate, as an oxidizing agent, which is substituted for m-chloroperbenzoic acid, as shown in the following Scheme 3.

Scheme 3



15 The processes according to Korean Patent Publication No. 92-3691 and US Patent No. 5,391,752 are described as producing omeprazole at yields of 96% and 81 to 92%, respectively. However, these patents include no mention of the N-oxide and sulfone by-products produced during the oxidation procedure, and also do not
20 clearly describe a purity of the produced omeprazole compound. Also, the disclosed processes employ a relatively complex purification procedure in which the product is extracted several times with methylene
25 chloride or chloroform, an environmentally harmful halogenated organic solvent, concentrated under vacuum, and then recrystallized.

Meanwhile, processes were recently reported which comprise oxidizing the sulfide compound of the formula
30 II with an oxidizing agent, such as hydrogen peroxide (H_2O_2), in the presence of a catalyst. However, these

processes are limited in kind of the catalyst used.

Korean Patent No. 100796 (1996) discloses a process for preparing the sulfoxide compound of the formula I by oxidizing the sulfide compound of the formula II with hydrogen peroxide in the presence of a vanadium catalyst. This process is described as producing the end compound at a high yield of 89.5 to 93.2 while inhibiting a production of the N-oxide byproduct at a low level.

However, the process according to the latter patent involves several problems when being applied for the industrial purpose. First, the specification of the disclosed patent mentions only the N-oxide by-product III, but includes no mention of whether the sulfone by-product IV as indicated in Scheme 2 is produced. Also, the specification does not mention a method of removing the sulfone by-product IV. However, in the preparation of highly pure medicaments, the by-products generally reduce a purity and stability of the end compound and, in some cases, can lead to discoloration of the end compound and also cause a undesirable pharmacological action in a human body. For this reason, tolerance of the by-products is strictly limited. It is generally well known that the oxidation reaction produces the sulfone by-product IV. WO 98/09962 (1998), WO 99/02521 (1999) and Spanish Patent No. 2,060,541 (1994) disclose processes for producing the sulfoxide compound I by an oxidation of the sulfide compound II. But the disclosed processes are problematic in that some of the produced sulfoxide compound is oxidized again to produce the sulfone compound IV. A chemical process is not known up to now, which can basically prevent a production of the

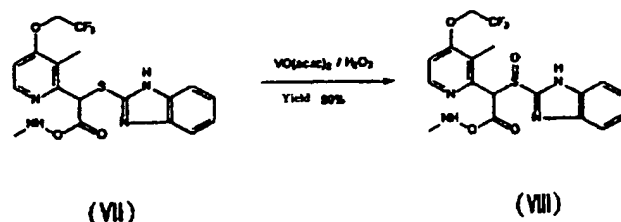
sulfone compound IV. The inventors of the present invention have practically repeated Example of Korean Patent No. 100796 (1996). Namely, according to the procedure of Example 4 of the latter patent producing
5 the end compound at the highest purity, a reaction was carried out for 5 hours. When the resulting reaction mixture was analyzed by HPLC, it was found that the sulfone compound was produced at the amount of more than about 1% (by HPLC area percent), and it remained at the
10 amount of about 0.4% even after the mixture was purified by isolation. In addition, it could be confirmed that domestically sold sulfoxide compounds have contained the sulfone compound at the amount of 0.1 to 0.2% (by HPLC area percent). As described above, since the sulfone
15 compound is very similar in physical and chemical properties to those of the sulfoxide compound, it is not easy to achieve the isolation for obtaining only the sulfoxide compound of a high purity. Second, the vanadium compound used as a catalyst is highly poisonous
20 to a human body and is not easy to handle, so that it is not suitable for use in mass production (US Patent No. 5,391,752). Third, the above described prior processes employs a complex purification procedure to remove by-products. Namely, the purification procedure according
25 to the prior processes comprises heating a crude crystal obtained after a reaction for obtaining the end compound to 60-70 °C to dissolve the crude crystal, filtering the solution to remove insoluble material, and recrystallizing the solution. Thus, it is difficult for
30 the prior processes to be applied for mass production due to an increase in working processes and a rising in manufacturing-costs. Fourth, the prior processes

disadvantageously results in the formation of a colored reaction mixture during the oxidation procedure, and thus further require a decoloring step of the reaction mixture, additionally to the purification procedure. It is generally well known that benzimidazole compounds are instable under acidic conditions so that they are discolored under oxidation conditions. For this reason, the prior processes additionally require the decoloring step (WO 98/40377 and 98/40378, and US Patent No. 5,374,730).

In addition to the above processes, several processes were proposed in which the sulfide compound II is oxidized with hydrogen peroxide in the presence of the vanadium compound acting as a catalyst.

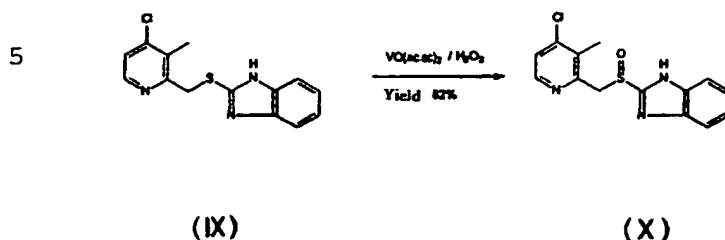
For example, US Patent Nos. 5,502,195 (1996) and 5,374,730 (1994) disclose a process for preparing a sulfoxide compound of the formula VIII from a compound of the formula VII, as indicated in the following Scheme 4.

Scheme 4



Moreover, Spanish Patent No. 2,060,541 (1994) discloses a process for preparing a compound of the formula X from a compound of the formula IX, as shown in the following Scheme 5.

Scheme 5



10 Spanish Patent No. 2,036,948 (1993) discloses a process which comprises oxidizing the sulfide compound with hydrogen peroxide in the presence of ammonium molybdate $[(\text{NH}_4)_2\text{MoO}_4]$, a molybdenum compound, which is substituted for the vanadium compound catalyst. However, 15 this process produces a sulfoxide compound at a low yield of 75% and thus is disadvantageous in view of the economical efficiency.

Among the prior catalysts proposed to use in the oxidation reaction according to the prior processes as 20 described above, only the vanadium compound is used up to now. However, the processes using the vanadium compound catalyst involve several problems when being applied for industrial purposes, as described above regarding Korean Patent No. 100796 (1996). Also, the 25 processes using other catalysts appear to be disadvantageous in view of the economical efficiency due to low yield.

As described above, the prior processes for preparing the sulfoxide compound disadvantageously 30 produce the N-oxide by-product III and the sulfone by-

product IV during the oxidation step. This makes the isolation and purification of a pure sulfoxide compound difficult. Another drawback with the prior processes is that they require the complex purification procedure including an additional decoloring step which is required due to the formation of the colored product. In addition, the prior processes are problematic in that they employ an environmentally harmful catalyst, or a catalyst or oxidizing agent poisonous to a human body, thereby involving a difficult when being applied for mass production.

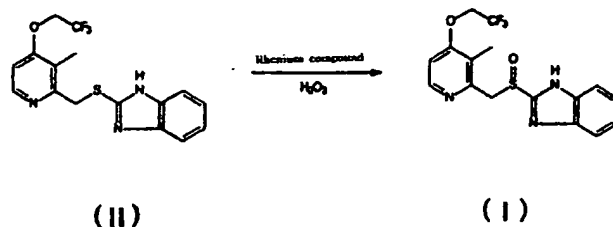
DISCLOSURE OF INVENTION

We have conducted systematic studies over a lengthy period of time to develop an industrially easily applied process by selecting a catalyst capable of minimizing a production of by-products such as a N-oxide compound of the formula III and a sulfone compound of the formula IV, and by selecting an environmentally harmless solvent, and also by eliminating a complex purification procedure. As a result of that, we found that, where a sulfide compound of the formula II is oxidized with hydrogen peroxide in the presence of a rhenium compound, a sulfoxide compound of the formula II is obtained at a high purity and yield by only a simple isolation procedure. Based on this discovery, we have perfected the present invention.

The present invention is directed to a process for preparing a sulfoxide compound of the formula I, which comprises the step of oxidizing a sulfide compound of the formula II with hydrogen peroxide as an oxidizing

agent, in an ethanol solvent, in the presence of a rhenium compound as a catalyst. The process of the present invention is illustrated in the following Scheme 6.

5 Scheme 6



10

Unlike the prior processes, the process according to the present invention minimizes a production of the N-oxide by-product III and the sulfone by-product IV while removing the by-products by only a simple isolation step, i.e., a filtration step, thereby producing the sulfoxide compound I at a high purity and yield.

BEST MODE FOR CARRYING OUT THE INVENTION

20 The present invention will now be described in detail.

Examples of the rhenium compound used as the catalyst in the practice of the present invention include methyltrioxorhenium, ethyltrioxorhenium, 25 $Re(PPh_3)_2OCl_3$ and the like. The most preferred catalyst is methyltrioxorhenium (CH_3ReO_3 ; commercially available from CAS Corp., Korea).

Methyltrioxorhenium was first reported by Hermann et al. to be a catalyst efficient for epoxidation of

olefinic compounds with hydrogen peroxide (Angew, Chem., Int. Ed. Engl., 30, 1636 (1991)). This methyltrioxorhenium is known as activating hydrogen peroxide, an oxygen source for an oxidizing agent, by an electrophilic reaction mechanism. In particular, unlike oxidizing agents used at approximately one equivalent amount or excess equivalent amounts, the methyltrioxorhenium catalyst has a significant advantage in that it is used for oxidation of a reactant without producing by-products. Further, it was recently reported that methyltrioxorhenium was excellent in its solubility in water and also in most of organic solvents, so that it was easy to isolate from the end compound (Espenson, J. H., Chem. Commun., 479-488, 1999). In view of the industrial application, the rhenium compound has advantages in that it is non-toxic to a human body and also shows a very high stability in air so that it is easy to store, handle and weigh. The rhenium compound is used at the amount of 0.1 to 10 mole %, and preferably 1 to 5 mole % relative to the compound of the formula II. Hydrogen peroxide as an oxygen source for an oxidizing agent is generally used in aqueous solution. In this case, hydrogen peroxide is preferably used at a concentration converted by a titration method. Also, hydrogen peroxide is used at the amount of 0.9 to 2 equivalents, and preferably 1 to 1.3 equivalents per one equivalent of the compound II. Examples of the organic solvents used in the practice of the present invention include alcoholic solvents such as methanol, ethanol, isopropanol, butanol, and the like. The preferred solvents are methanol and ethanol. These alcoholic solvents may be used alone or in admixture with water.

In the latter case, the volume ratio of water to alcoholic solvent is in the range of 1:5 to 1:15, and preferably 1:8 to 1:10. The oxidation according to the present invention is carried out at a temperature of -40 °C to 0 °C and preferably -30°C to -15 °C, for 1 to 10 hours and preferably 3 to 7 hours. The reaction mixture produced under the oxidation conditions as described above contains the N-oxide compound III at the amount of less than 0.06% (by HPLC area percent) and the sulfone compound IV at the amount of less than 0.06% (by HPLC area percent), additionally to the sulfoxide compound of the formula I. On the other hand, the prior art (Korean Patent No. 100796) produces the N-oxide by-product at the amount of about 0.2% and the sulfone by-product at the amount of about 1%. Accordingly, it could be found that the oxidation conditions of the present invention were excellent as compared to those of the prior art. Meanwhile, during the oxidation according to the present invention, the sulfoxide compound I is mostly deposited in the form of crystal. Thus, in the process according to the present invention, the conventional isolation procedures, for example, extraction, decoloration and recrystallization are not required to isolate the end compound. In other words, in the process of the present invention, aqueous sodium thiosulfate solution is added to the deposited crystal to decompose the remaining hydrogen peroxide. After this, the resulting mixture is filtered and washed with the appropriate alcoholic solvent as described above to give the sulfoxide compound of the formula I at a high purity and yield.

The preparing process of the present invention inhibits a production of the N-oxide compound II to less

than 0.05% (by HPLC area percent) and a production of the sulfone compound IV to 0% (by HPLC area percent). Thus, the process of the present invention can prepare the sulfoxide compound at a high purity of more than
5 99.95% (by HPLC area percent) and a high yield of more than 90%.

Advantages of the process according to the present invention can be summarized as follows: First, the prior art employs a dangerous material, or an oxidizing agent
10 and catalyst poisonous to a human body, whereas the process of the present invention utilizes the rhenium compound which is harmless to a human body and easy to store and handle. Thus, the process of the present invention can be easily applied for mass production.
15 Second, the process of the present invention minimizes a production of the N-oxide and sulfone by-products as compared to that of the prior art, and thus can produce the end compound at a high purity of 99.95 % or more (by HPLC area percent) and a high yield of 90% or more.
20 Third, the process of the present invention eliminates the use of the environmentally harmful halogenated solvent while employing the environmentally harmless ethanol solvent. Fourth, to obtain the sulfoxide compound of a high purity, the prior art requires a
25 complex purification procedure, such as extraction, decoloration, recrystallization and the like, whereas the present invention allows the end compound to be obtained at a high purity by simply filtering and washing a crystal produced after the reaction. This
30 ensures that the present invention is easily applied for mass production and economically carried out.

The following examples are for further

illustration purposes only and in no way limit the scope of this invention.

Example 1: Preparation of 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyrid-2-yl]methylsulfinyl]benzimidazole

5 1.0 g (2.7 mmol) of 2-[[3-methyl-4-trifluoroethoxy]pyrid-2-yl]methylthio]benzimidazole monohydrate was dissolved in 20 ml of 95% ethanol and cooled to a temperature of -20 to -30 °C. Then, 26.4 mg of methyltrioxorhenium and 0.31 g (2.7 mmol) of a 30%
10 aqueous hydrogen peroxide solution were added, and stirred for 5 hours at the same temperature. Completion of the reaction was monitored by TLC and HPLC. To the reaction mixture produced as a crystal, was added an aqueous sodium thiosulfate solution (1 g/10 ml) and
15 isopropanol (10 ml), and then stirred for 1 hour while cooling with ice. The reaction mixture was filtered to isolate a crystal, washed with an ice-cooled isopropanol:water mixture (1:1), and then dried under vacuum to give 0.94 g (94.4% yield) of the title
20 compound as a white solid. Melting point: 177-180 (decomposition).

Comparative Example 1: Preparation of 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyrid-2-yl]methylsulfinyl]benzimidazole

25 1.0 g (2.7 mmol) of 2-[[3-methyl-4-trifluoroethoxy]pyrid-2-yl]methylthio]benzimidazole monohydrate was dissolved in 10 ml of 95% methanol and cooled to a temperature of -20 to -30 °C. Then, 26.4 mg of methyltrioxorhenium and 0.31 g (2.7 mmol) of an
30 aqueous 30% hydrogen peroxide solution were added, and

stirred for 5 hours at the same temperature. Completion of the reaction was monitored by TLC and HPLC. To the reaction mixture produced as a crystal, was added an aqueous sodium thiosulfate solution (1 g/10 ml) and isopropanol (10 ml), and then stirred for 1 hour while cooling with ice. The reaction mixture was filtered to isolate a crystal, washed with an ice-cooled isopropanol:water mixture (1:1), and then dried under vacuum to give 0.89 g (89.6% yield) of the title compound as a white solid.

Comparative Example 2: Preparation of 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyrid-2-yl]methylsulfinyl]benzimidazole

1.0 g (2.7 mmol) of 2-[[3-methyl-4-trifluoroethoxy]pyrid-2-yl]methylthio]benzimidazole monohydrate was dissolved in 20 ml of an ethanol:water mixture (9:1) and cooled to a temperature of -20 to -30 °C. Then, 26.4 mg of methyltrioxorhenium and 0.31 g (2.7 mmol) of an aqueous 30% hydrogen peroxide solution were added, and stirred for 5 hours at the same temperature. Completion of the reaction was monitored by TLC and HPLC. To the reaction mixture produced as a crystal, was added an aqueous sodium thiosulfate solution (1 g/10 ml) and isopropanol (10 ml), and then stirred for 1 hour while cooling with ice. The reaction mixture was filtered to isolate a crystal, washed with an ice-cooled isopropanol:water mixture (1:1), and then dried under vacuum to give 0.90 g (90.7% yield) of the title compound as a white solid.

Comparative Example 3: Preparation of 2-[[3-

methyl-4-(2,2,2-trifluoroethoxy)pyrid-2-yl)methylsulfinyl]benzimidazole

1.0 g (2.7 mmol) of 2-[[3-methyl-4-trifluoroethoxy]pyrid-2-yl)methylthio]benzimidazole monohydrate was dissolved in 20 ml of 95% ethanol and cooled to a temperature of -20 to -30 °C. Then, 3.3 mg of methyltrioxorhenium and 0.31 g (2.7 mmol) of an aqueous 30% hydrogen peroxide solution were added, and stirred for 5 hours at the same temperature. Completion of the reaction was monitored by TLC and HPLC. To the reaction mixture produced as a crystal, was added an aqueous sodium thiosulfate solution (1 g/10 ml) and isopropanol (10 ml), and then stirred for 1 hour while cooling with ice. The reaction mixture was filtered to isolate a crystal, washed with an ice-cooled isopropanol:water mixture (1:1), and then dried under vacuum to give 0.89 g (89.6% yield) of the title compound as a white solid.

Table 1 shows a comparison of products from Example 1, Comparatives 1-3 and the prior art (Korean Patent No. 100796) in terms of yield and purity (by HPLC area percent). HPLC conditions used for the purity analysis are as follows:

Apparatus used: Jasco PU-1580 High Speed Liquid Chromatography

Detector: Jasco UV-1575 UV Absorption Spectrophotometer

Wavelength: 285 nm

Column: Mightsil RP-18GP (250 x 4.6 mm, 5 µm)

Mobile phase: Acetonitrile: water: triethylamine mixture (40: 60: 10) (adjusted to pH 7 with phosphoric acid)

Flow rate: 1.0 ml/minute

Column temperature: Constant temperature of about 25 °C.

Table 1: Comparison of Example 1 with the prior art in terms of yield and purity

	Example 1	Comparative Example 1	Comparative Example 2	Comparative Example 1	Korean Pat. No. 100796; Example 4
Yield (%)	94.40%	89.60%	90.70%	89.60%	91.00%
Area % of Compound I	99.95%	99.71%	99.80%	99.82%	99.70%
Area % of Compound III	0.05%	0.08%	0.06%	0.06%	<0.1%
Area % of Compound IV	0.00%	0.21%	0.14%	0.12%	0.41% ^a

^a 0.41% was measured by the inventors from a product obtained by repeating Example 4 of Korean Patent No. 100796 which showed that the end compound had the highest purity. However, the specification of the latter patent includes no mention of the sulfone compound IV.

As indicated in Table 1, Example 1 using ethanol as a solvent showed an excellent yield compared to Comparative Examples 1-3 using methanol or a mixture of ethanol and water as the solvent. Also, it could be found that, when the methyltrioxorhenium catalyst was used at the amount of 1 mole% or less, yield was decreased.

Moreover, when comparing Example 1 of the present invention and Example 4 of Korean Patent No. 100796 in terms of the by-product production percent and the end compound purity, it could be found that Example 1 showed a higher purity than Example 4 of the prior art (Korean Patent No. 100796). In particular, from the fact that Example 1 showed a sulfone compound area percent of 0 %, it can be found that the process of the present

invention produced no sulfone by-product and thus produced the sulfoxide compound I at a higher yield compared to Comparative Examples 1-3 and the prior art. In addition, the process of the present invention could
5 be found to be an excellent process capable of basically preventing the sulfone by-product production.

INDUSTRIAL APPLICABILITY

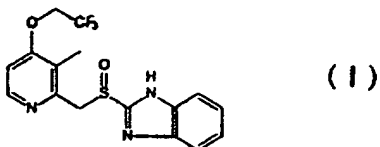
As apparent from the foregoing, the process
10 according to the present invention minimizes a production of by-products by conducting the oxidation of the sulfide compound with hydrogen peroxide in the presence of the methyltrioxorhenium catalyst which is harmless to a human body and is easy to store and
15 handle. Also, the process of the present invention can produce the sulfoxide compound useful as anti-ulcer agents at a high yield and purity by only a simple filtration without a need of the complex procedure or the decoloring step. In addition, the process of the
20 present invention is easily applied for mass production and thus is useful in the industrial and economical views.

Although the preferred embodiments of the invention have been disclosed for illustrative purposes,
25 those skilled in the art will appreciate that various modifications, additions and substitutions are possible, without departing from the scope and spirit of the invention as disclosed in the accompanying claims.

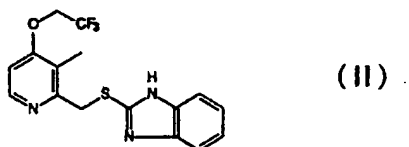
WHAT IS CLAIMED IS:

1. Process for preparing a sulfoxide compound of the formula I, which comprises the step of reacting a sulfide compound of the formula II with hydrogen peroxide in an ethanol solvent in the presence of a rhenium compound of 1 to 5 mole% relative to the sulfide compound II:

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2. The process of Claim 1, in which the rhenium compound is methyltrioxorhenium.

3. The process of Claim 2, further comprising the step of filtrating a product obtained after the reaction step to remove by-products, thereby obtaining the sulfoxide compound at a high yield and purity.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR00/01019

A. CLASSIFICATION OF SUBJECT MATTER

IPC7 C07D 401/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean Patents and applications for inventions since 1975

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ON LINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5374730 A (Torcan Chemical Ltd.) 20 Dec.1994 See the whole document	1-3
A	EP 0302720 A (Takeda Chemical Industries, Ltd) 8 Feb 1989 See the whole document	1-3
A	Arterburn J. B. and Nelson S. L. 'Rhenium-catalyzed oxidation of sulfides with phenyl sulfoxide' In J. Org.Chem. 1996, Vol.61(7), p2260-2261.	1-3

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30 DECEMBER 2000 (30.12.2000)

Date of mailing of the international search report

30 DECEMBER 2000 (30.12.2000)

Name and mailing address of the ISA/KR

Korean Industrial Property Office
Government Complex-Taejon, Dunsan-dong, So-ku, Taejon
Metropolitan City 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

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CHO, Myung Sun

Telephone No. 82-42-481-5605



INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR00/01019

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5374730 A	20.12.1994	EP 0724582 A. CA 2170250 A WO 9512590 A	07.08.1996 11.05.1995 11.05.1995
EP 0302720 A	08.02.1989	CA 1263119 A JP 6086444 B KR 9600047 B US 5578732 A	21.11.1989 02.11.1994 03.01.1996 26.11.1996